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VIA ELECTRONIC SUBMISSION AND HAND DELIVERY

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket No. FDA-2018-N-3552 ("Agency Information Collection Activities; Proposed Collection; Comment Request; Experimental Study of Cigarette Warnings")

Dear Sir or Madam,

On September 26, 2018, the U.S. Food and Drug Administration ("FDA" or "the Agency") published a notice soliciting comments on an experimental study of cigarette warnings that is being conducted in support of the graphic-warnings provision of the Family Smoking Prevention and Tobacco Control Act. *See Agency Information Collection Activities; Proposed Collection; Comment Request; Experimental Study of Cigarette Warnings*, 83 Fed. Reg. 48,625 (Sept. 26, 2018). In response, RAI Services Company ("RAIS") respectfully submits these comments on its own behalf and on behalf of its affiliated tobacco companies.[1] RAIS is committed to working cooperatively with FDA to address important public health issues regarding tobacco use in this country, including through appropriate warnings on tobacco products.

According to the September 26 notice, the Agency plans to conduct a "voluntary online experiment" that will "assess whether new cigarette warnings increase public understanding of the negative health consequences of cigarette smoking." *Id.* at 48,626. The study involves 17 treatment conditions—one condition in which participants will view "one of the four current Surgeon General's warnings" and 16 conditions in which participants will view one "graphic

[1] RAIS coordinates regulatory compliance for Reynolds American Inc.'s subsidiary companies, including R.J. Reynolds Tobacco Company, American Snuff Company, LLC, Santa Fe Natural Tobacco Company, Inc., Kentucky BioProcessing, Inc., and R.J. Reynolds Vapor Company. References to RAIS in this letter include itself and its affiliated RAI subsidiaries as applicable.

health warning, containing a warning statement accompanied by a concordant color graphic depicting the negative health consequences of smoking described in the statement." *Id.* at 48,627.

FDA has explained that the study will occur in three sessions. In the first, participants will "complete a baseline assessment about their beliefs about the negative health consequences of cigarette smoking," view one of the warnings discussed above, and then complete another assessment. *Id.* In the second session (one to two days later), participants will view the same warning, and complete another assessment. *Id.* And in the third session (approximately 14 days later), participants "will complete a delayed post-test on beliefs about the negative health consequences caused by cigarette smoking and items assessing recall of the warning." *Id.*

FDA has invited comments on (among other things) the "practical utility" of the information to be collected and "ways to enhance the quality, utility, and clarity" of that information. *Id.* at 48,626. In response to this invitation, RAIS offers the following comments.

First, as designed, this study does not help FDA satisfy the requirements of the First Amendment. Because a graphic-warnings rule would compel manufacturers to express the government's preferred message, the rule would be subject to First Amendment scrutiny. And no matter which First Amendment test applies, FDA has a constitutional duty to consider less-burdensome alternatives. Yet FDA has failed to do so. Indeed, as the study design shows, FDA is not testing any alternatives to a graphic-warnings rule, such as (1) changes to the size and placement of the existing warnings, (2) new textual warnings without graphic images, or (3) new textual warnings with graphic images that have a less-intrusive size and placement. For example, it is far from clear that FDA has considered whether the burdensome use of large, duplicative (front/back of pack) warnings is needed. In addition, FDA has not identified a "substantial" interest that this current iteration of a graphic-warnings rule serves. FDA says that the "purpose of the study is to assess whether new cigarette warnings increase public understanding of the negative health consequences of cigarette smoking." *Id.* But FDA does not have a substantial interest simply in "increasing public understanding." And even if that interest were substantial, the graphic warnings would not materially advance that interest, given that the public already understands that smoking cigarettes causes serious diseases and harms one's health.

Second, FDA has provided little detail about the study's design, which makes it impossible for the public to reasonably assess the design and provide meaningful comments. For example, FDA has shared neither the text nor the graphics of the new warnings it proposes to test. As another example, FDA has not published the questions that it plans to ask the participants—even though a study's validity and reliability depend on what participants are told about the research, how the questions are framed, and the order in which those questions are asked. This lack of detail has substantially—and unfairly—limited the public's ability to comment on the study. For these reasons, RAIS believes that FDA must provide further details regarding this study, and then provide another opportunity for public comment.

Third, the limited information that FDA has released suggests that FDA's study contains numerous methodological flaws that will overstate the effectiveness of the graphic warnings. For example: (a) the sample size for each condition appears to be quite small; (b) the study is a "voluntary online experiment," which creates the risk of selection bias and a sample population that does not adequately mirror the relevant portions of the U.S. population; (c) the questions that

FDA plans to ask create a serious risk of bias; (d) the study does not appear to adequately mimic real-world conditions; (e) the study appears to lack meaningful pretesting; and (f) FDA has not explained how it will mitigate the problem of social-desirability bias.

These comments set forth RAIS's views on these First Amendment problems and methodological flaws. In order to ensure that the information to be collected has "practical utility" and to enhance the "quality, utility, and clarity" of that information (*id.*), FDA should modify its study as set forth below.

COMMENTS

I. AS DESIGNED, THE GRAPHIC-WARNINGS STUDY DOES NOT HELP FDA SATISFY THE REQUIREMENTS OF THE FIRST AMENDMENT.

A. The study will not examine whether FDA could increase public understanding in a less-burdensome manner.

1. "Since *all* speech inherently involves choices of what to say and what to leave unsaid, one important manifestation of the principle of free speech is that one who chooses to speak may also decide what not to say." *Hurley v. Irish-Am. Gay, Lesbian & Bisexual Grp. of Boston*, 515 U.S. 557, 573 (1995) (citations and quotation marks omitted). Thus, the "general rule" is that the government "may not compel affirmance of a belief with which the speaker disagrees." *Id.* This rule "applies not only to expressions of value, opinion, or endorsement, but equally to statements of fact the speaker would rather avoid." *Id.* And it applies to "ordinary people" and "business corporations" alike. *Id.* at 574; *see also Pac. Gas & Elec. Co. v. Pub. Utils. Comm'n*, 475 U.S. 1, 16 (1986) (plurality op.) ("For corporations as for individuals, the choice to speak includes within it the choice of what not to say.").

In light of these principles, courts generally apply strict scrutiny to government-compelled speech. *See, e.g.*, *Wooley v. Maynard*, 430 U.S. 705, 714–15 (1977). Under strict scrutiny, the government must prove that the compulsion "furthers a compelling interest and is narrowly tailored to achieve that interest." *Reed v. Town of Gilbert*, 135 S. Ct. 2218, 2231 (2015).

In the commercial context, there are two situations in which courts sometimes apply a lower standard of scrutiny. *First*, the government may require "purely factual and uncontroversial" commercial disclosures, provided they are not "unjustified or unduly burdensome." *Zauderer v. Office of Disciplinary Counsel*, 471 U.S. 626, 651 (1985). *Second*, some courts have suggested that the government may compel commercial speech if (1) its asserted interest is substantial, (2) the compulsion directly and materially advances that interest, and (3) the compulsion is narrowly tailored. *See Cent. Hudson Gas & Elec. Corp. v. Pub. Serv. Comm'n*, 447 U.S. 557, 566 (1980). Under the narrow-tailoring prong, "if the Government could achieve its interests in a manner that does not restrict speech, or that restricts less speech, the Government must do so." *Thompson v. W. States Med. Ctr.*, 535 U.S. 357, 371 (2002).

Under all three of these standards—strict scrutiny, *Zauderer*, and *Central Hudson*—the government must consider whether it could achieve its aims in a less-burdensome way. Thus, "[a]lthough the standard for assessing burdens on commercial speech has varied, the Supreme Court's bottom line is clear: the government must affirmatively demonstrate its means are

'narrowly tailored' to achieve a substantial government goal." *See United States v. Philip Morris USA Inc.*, 566 F.3d 1095, 1143 (D.C. Cir. 2009) (per curiam) (citations omitted).

Here, a graphic-warnings rule would compel manufacturers to express the government's preferred message. *See R.J. Reynolds Tobacco Co. v. FDA*, 696 F.3d 1205, 1211 (D.C. Cir. 2012) (holding that FDA's initial graphic-warnings rule "contain[ed] elements of compulsion and forced subsidization" and was therefore subject to First Amendment scrutiny), *overruled in part by Am. Meat Inst. v. U.S. Dep't of Agric.*, 760 F.3d 18, 31 (D.C. Cir. 2014) (en banc). The graphic-warnings rule is therefore subject to First Amendment scrutiny, which necessarily requires FDA to consider less-burdensome alternatives.

2. As FDA's study design shows, however, FDA has failed to fulfill that constitutional duty. The September 26 notice suggests that the purpose of a graphic-warnings rule is to "increase public understanding of the negative health consequences of cigarette smoking." 83 Fed. Reg. at 48,626. Although FDA could advance that interest in several different ways, the study will not test even a single alternative.

Most importantly, FDA's study will not test whether FDA could increase public understanding by making less-burdensome changes to the existing warnings. The Tobacco Control Act changed the existing warnings in several ways: it created nine new textual warnings, 15 U.S.C. § 1333(a)(1); it required that the warnings appear "in the upper portion of the front and rear panels of the package," *id.* § 1333(a)(2); it required that the label "comprise the top 50 percent of the front and rear panels of the package," *id.*; and it required that FDA create "color graphics depicting the negative health consequences of smoking to accompany the label statements specified in subsection (a)(1)," *id.* § 1533(d). As a result, FDA could select one or more of these possible changes to fashion a less-burdensome alternative to a graphic-warnings rule. FDA could, for example, require that manufacturers replace the existing Surgeon General's warnings with the new textual warnings. Or FDA could require that manufacturers use the new textual warnings *and* place them at the top of the package. Either of these examples would be less-burdensome than a graphic-warnings rule.

If FDA wanted to fulfill its constitutional duty to consider these alternatives, FDA could easily design a study that examines their effects independently. For example, FDA could show one group of participants a package with the current Surgeon General's warnings, and show another group a package that alters the size and placement of those warnings. That would allow FDA to determine the extent to which changing the size and placement contributes, if at all, to an increase in public understanding. As another example, FDA could show one group of participants a package with the current Surgeon General's warnings, show 16 groups a package with the new textual warnings, and show 16 more groups a package with the new textual warnings *and* graphic images. That would allow FDA to determine how much the graphic images contribute, if at all, to FDA's stated goal. In other words, consistent with the requirements of the First Amendment, FDA should have designed a study that determines the marginal impact of several different changes to the existing warnings, and then selected the least-burdensome approach.

But FDA has not done so. Instead, FDA plans to show one group of participants advertising and packaging with the current Surgeon General's warnings, and then show 16 groups of participants advertising and packaging with both a new textual warning *and* a graphic image. *See*

83 Fed. Reg. at 48,627. This study design will make it impossible for FDA to isolate the (potential) effects of the changes in size and placement, the new textual warnings, and the graphic images. By failing to consider these obvious less-burdensome alternatives, FDA's study does not help the Agency satisfy the First Amendment.

B. FDA has not identified a substantial interest that a graphic-warnings rule would serve.

Under any standard of First Amendment scrutiny, FDA must have at least a "substantial" interest before compelling speech. *See Reed*, 135 S. Ct. at 2231 (strict scrutiny requires a "compelling" interest); *Cent. Hudson*, 447 U.S. at 566 (requiring a "substantial" interest); *Am. Meat*, 760 F.3d at 34 (Kavanaugh, J., concurring in the judgment) (*Zauderer* requires a "substantial" interest). But FDA has not explained what interest the graphic warnings would serve, much less demonstrated that such an interest is "substantial." As the D.C. Circuit has explained, any interest that FDA has in increasing public understanding is not in and of itself "substantial" for First Amendment purposes. And even if it were, the graphic warnings would not advance that interest because the public already understands that smoking cigarettes can cause serious diseases and harm one's health.

1. The September 26 notice says that the "purpose of the study is to assess whether new cigarette warnings increase public understanding of the negative health consequences of cigarette smoking." 83 Fed. Reg. at 48,626. FDA seemingly has designed the study to measure outcomes that are related to that purpose. Specifically, "[s]tudy outcomes include comparisons to assess the extent to which exposure to the graphic health warnings, relative to the text-only Surgeon General's warnings, provide new information, increase self-reported learning, change beliefs about the negative health consequences of cigarette smoking, increase thinking about the risks of smoking, as well as the extent to which the warnings are informative, easy to understand, factual, attention grabbing, and recalled." *Id.* at 48,627.

But FDA does not have a substantial interest in "increasing public understanding." As then-Judge Kavanaugh has explained, "[f]or *Central Hudson* purposes … it is plainly not enough for the Government to say simply that it has a substantial interest in giving consumers information." *Am. Meat*, 760 F.3d at 31 (Kavanaugh, J., concurring in the judgment). "After all, that would be true of any and all disclosure requirements." *Id.* Thus, allowing the government to compel speech merely to increase public understanding "would drain the *Central Hudson* test of any meaning in the context of compelled commercial disclosures." *Id.*

The D.C. Circuit reached the same conclusion the last time that FDA issued a graphic-warnings rule. There, "FDA assert[ed] an interest in 'effectively communicating health information' regarding the negative effects of cigarettes." *R.J. Reynolds Tobacco Co.*, 696 F.3d at 1221. The court concluded, however, that FDA's "attempt to reformulate its interest as purely informational is unconvincing, as an interest in 'effective' communication is too vague to stand on its own." *Id.* The court further held that "FDA's interest in 'effectively communicating' the health risks of smoking is merely a description of the means by which it plans to accomplish its goal of reducing smoking rates, and not an independent interest capable of sustaining the Rule." *Id.*

2. Moreover, even if "increasing public information" were a substantial interest, FDA would need to show that the graphic warnings advanced that interest "to a material degree." *Edenfield v. Fane*, 507 U.S. 761, 771 (1993). Because the public already understands that smoking cigarettes can cause serious diseases and harm one's health, FDA could not possibly satisfy that burden.

For decades, cigarette manufacturers have warned the public that cigarette smoking can cause serious diseases and harm one's health. In 1965, Congress mandated that cigarette packages include warning labels. Federal Cigarette Labeling and Advertising Act, Pub. L. No. 89-92, 79 Stat. 282 (1965). In 1970, Congress adopted a new warning: "Warning: The Surgeon General Has Determined That Cigarette Smoking Is Dangerous to Your Health." Public Health Cigarette Smoking Act of 1969, Pub. L. No. 91-222, 84 Stat. 87 (1970). In Congress's view, this warning fully advised the public about the risk of smoking; thus, Congress provided that "[n]o statement relating to smoking and health, other than [this warning], shall be required on any cigarette package." *Id.* at 88. And in 1984, Congress required that all packaging and advertising include a series of rotating warnings that covered a variety of smoking risks:

- "SURGEON GENERAL'S WARNING: Smoking Causes Lung Cancer, Heart Disease, Emphysema, And May Complicate Pregnancy.
- "SURGEON GENERAL'S WARNING: Quitting Smoking Now Greatly Reduces Serious Risks to Your Health.
- "SURGEON GENERAL'S WARNING: Smoking By Pregnant Women May Result in Fetal Injury, Premature Birth, And Low Birth Weight.
- "SURGEON GENERAL'S WARNING: Cigarette Smoke Contains Carbon Monoxide."

Comprehensive Smoking Education Act, Pub. L. No. 98-474, 98 Stat. 2200, 2201–02 (1984). These warnings likewise preempted all other warnings. *See* 15 U.S.C. § 1334 (1988).

The government and other organizations (such as the American Cancer Society and the American Lung Association) have also engaged in public health campaigns urging smokers to quit. For example, between 2009 and 2014, FDA spent more than $500 million on such campaigns. U.S. Gov't Accountability Office, *Most FDA Spending Funded Public Education, Regulatory Science, and Compliance and Enforcement Activities*, No. 14-561, at 22–25 (June 2014), https://tinyurl.com/y93gktex.[2] And between 2014 and 2016, FDA spent more than $240 million on "The Real Cost" advertising, which was aimed at preventing youth tobacco use. Anna J. MacMonegle et al., *Cost-Effectiveness Analysis of The Real Cost Campaign's Effect on Smoking Prevention*, 55 Am. J. of Preventative Med. 319, 323 (2018), https://tinyurl.com/yb5xfxcg.

As a result of these warning labels and public health campaigns, public awareness about the health risks of smoking cigarettes is effectively universal. According to Gallup polls taken

[2] All web addresses in these comments have been shortened using a URL shortener, which results in a web address that contains "tinyurl."

every year since 2002,[3] between 93% and 97% of Americans are aware that smoking is harmful. Gallup, *Tobacco and Smoking* (last visited Oct. 22, 2018), https://tinyurl.com/y94xlly3. And after only 8 months of advertising, more than 90% of "The Real Cost" campaign's target audience were aware of the campaign and its message. MacMonegle et al., *supra*, at 320; FDA, *FY 2018 FDA Budget Tobacco Control Act* at 191–92, https://tinyurl.com/y7lfxre7.

Indeed, the public actually *overestimates* many of the risks from smoking. For example, "the average perceived risk that a smoker will develop lung cancer is over 40%," whereas the "actual risk" is "about 10%." Statement of W. Kip Viscusi, Docket No. FDA-2010-N-0568, at 25 (Jan. 11, 2011), https://tinyurl.com/ybtwkles. As another example, the public's perception of the overall mortality risk from smoking "can be as much as three times higher" than the actual mortality risk, and "young people overestimate the dangers of smoking to an even greater degree" than adults. *Id.* at 28–29.

Because the public already knows that smoking cigarettes can cause serious diseases and harm one's health, the graphic warnings would not increase public understanding "to a material degree." *Edenfield*, 507 U.S. at 771. Indeed, even if the graphic warnings advised the public of additional diseases caused by smoking, that would not meaningfully change the public's basic views about cigarettes. Thus, any interest that FDA has in "increasing public understanding" would not save a graphic-warnings rule.

3. In short, FDA has not identified a substantial interest that a graphic-warnings rule would serve. FDA's stated goal of increasing public understanding is not "substantial" for First Amendment purposes. And even if it were, FDA cannot advance that interest by reminding consumers of risks that they "already know"—or even overestimate. *Nat'l Inst. of Family & Life Advocates v. Becerra*, 138 S. Ct. 2361, 2377 (2018).

II. BEFORE CONDUCTING THE PROPOSED GRAPHIC-WARNINGS STUDY, FDA MUST PUBLISH ENOUGH INFORMATION TO ALLOW FOR MEANINGFUL PUBLIC INPUT.

FDA's notice invites comments on (among other things) the "practical utility" of the information to be collected and "ways to enhance the quality, utility, and clarity" of that information. 83 Fed. Reg. at 48,626. The notice fails, however, to provide crucial details that the public and impacted parties need in order to provide meaningful comments. To solve that problem, FDA must take two steps. *First*, before the study begins, FDA must publish additional information, including (a) a detailed statement explaining the interest that the graphic warnings would advance, (b) more detail regarding the sampling protocol and FDA's assessment of the generalizability of the study's results, (c) the study's complete protocol, including the statistical-analysis plan, the description of the study, and the questionnaire that will be used with study participants, and (d) the text and graphics that the Agency proposes to test. FDA must then give the public an opportunity to comment on this additional information. *Second*, after the study has been completed, FDA must quickly release the data generated by the study, so the public has adequate time to process, review,

[3] The one exception is 2009, in which no poll was taken.

and analyze that data *before* FDA issues a proposed rule. Unless the Agency takes these steps, the public simply cannot provide meaningful comments on FDA's study.

1. The Paperwork Reduction Act requires that, before collecting information, an agency must "provide 60-day notice in the Federal Register." 44 U.S.C. § 3506(c)(2)(A). The Act further requires that the notice must "solicit comment[s]" on (among other things) the "practical utility" of the information to be collected and ways to "enhance the quality, utility, and clarity" of that information. *Id.* And the Act requires that the agency "consult with members of the public" about the "proposed collection of information." *Id.* As these parts of the Act make clear, Congress has recognized that meaningful feedback from the public is critical to any agency's regulatory efforts.

Despite this congressional mandate, FDA has deprived the public of the chance to provide relevant feedback by withholding crucial details about the proposed graphic-warnings study. The September 26 notice says that "participants will complete a baseline assessment about their beliefs about the negative health consequences of cigarette smoking." 83 Fed. Reg. at 48,627. But FDA has not provided *any* information about the questions that the Agency plans to use in that baseline assessment. Likewise, FDA has not published the questionnaires that participants will complete after viewing the graphic warnings—even though those questionnaires are incredibly important in determining whether the study's results will be valid and reliable. The notice also does not explain how FDA plans to avoid various types of bias—such as selection, question-order, and social-desirability bias—that could taint the study's results. And most glaringly, the notice even fails to include the text and graphics that make up the warnings themselves—the very object of the study. Indeed, this omission is akin to the Environmental Protection Agency requesting comments on whether a proposed study on the effects of a greenhouse gas is likely to provide relevant data without disclosing the greenhouse gas that the Agency plans to evaluate. FDA offers no explanation at all for this stunning omission.

What's more, FDA's failure to provide the graphic warnings that it proposes to study is at odds with the Agency's past practice. Specifically, when the Agency proposed to study the textual warning statements that might accompany the graphic images, FDA published all 15 of those statements. *See Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request; Experimental Study on Warning Statements for Cigarette Graphic Health Warnings*, 82 Fed. Reg. 43,764 (Sept. 19, 2017). But here, FDA offers nothing but silence as to why it has chosen to hide the very subject of its proposed study. The purpose of the Paperwork Reduction Act—not to mention the bedrock obligation to engage in reasoned decisionmaking—requires more.

2. FDA's decision to withhold these crucial details would be problematic in any context. But this decision is especially troubling in the context of a graphic-warnings rule.

First, the Agency's initial attempt to develop a graphic-warnings rule failed in large part because FDA refused to listen to public feedback. In 2011, FDA issued a proposed rule requiring that cigarette packaging and advertisements bear one of nine graphic warnings, in addition to the phone number for the National Cancer Institute's "Network of Tobacco Cessation Quitlines" (1-800-QUIT-NOW). *See Required Warnings for Cigarette Packages and Advertisements*, 76 Fed. Reg. 36,628 (June 22, 2011). Several commenters—including academics, cancer researchers, nonprofits, and tobacco companies—critiqued the study on which FDA had relied when selecting

the graphic warnings. But time and time again, FDA dismissed those comments out of hand. Two commenters recommended that FDA "conduct longitudinal research or post-market surveillance to assess [the] actual long-term effects" of the warnings; FDA simply responded that the "existing scientific literature" was sufficient. *R.J. Reynolds Tobacco Co.*, 696 F.3d at 1210. Other commenters said that "FDA's research study failed to provide evidence that the proposed warnings would actually affect smoking rates, significantly affect consumers[']knowledge of the risks of smoking, or bring about actual behavior change." *Id.* But "FDA disagreed, again relying on" what it considered to be adequate evidence. *Id.* "Another comment asserted that the study's selection bias constituted a serious methodological flaw"; FDA simply "avoided the substance of this argument." *Id.* And several commenters criticized the "lack of statistical evidence supporting FDA's belief that requiring cigarette packages to bear the graphic warnings would reduce smoking rates." Yet "FDA summarily disagreed." *Id.*

FDA's refusal to listen to these commenters contributed directly to the rule's downfall. After FDA issued a final graphic-warnings rule, five tobacco companies, including R.J. Reynolds, challenged the rule in the U.S. District Court for the District of Columbia. *See R.J. Reynolds Tobacco Co. v. FDA*, 845 F. Supp. 2d 266 (D.D.C. 2012). The district court held that the rule violated the First Amendment by unconstitutionally compelling speech, and the U.S. Court of Appeals for the D.C. Circuit affirmed. *See R.J. Reynolds Tobacco Co.*, 696 F.3d at 1208. The D.C. Circuit held that, under the First Amendment, FDA had to identify "substantial evidence" that the rule would "directly advance [the Agency's] interest in reducing smoking rates to a material degree." *Id.* at 1220 (quotation marks omitted). But FDA did not have a "shred of evidence" that the graphic warnings would directly reduce the number of Americans who smoke. *Id.* at 1219. Instead, because FDA refused to listen to public feedback, the Agency was left with nothing but "mere speculation" and "questionable social science." *Id.*

Second, FDA's current attempt to develop a graphic-warnings rule has already run into problems with study design. In September 2017, FDA submitted to the Office of Management and Budget ("OMB") a proposed study on the textual warnings that the Agency intends to accompany the graphic images. In January 2018, OMB granted only a limited approval of that study. *See* OMB, *Notice of Office of Management and Budget Action, Experimental Study on Warning Statements for Cigarette Graphic Health Warnings*, Ref. No. 201708-0910-011 (Jan. 29, 2018), https://tinyurl.com/ybwk7ptv (hereinafter "OMB Terms of Clearance"). Specifically, OMB explained that, "[d]ue to the study design, convenience sampling methodology, and methods of analyses—significant limitations exist with regard to the generalizability of results from this study." *Id.* "Because of these limitations, the relationship between treatment and outcomes [that FDA] find[s] in [its] study *may not generalize to the broader U.S. population*." *Id.* (emphasis added). Thus, FDA had to "confirm[] that all such limitations inherent in the study design and methodology will be communicated in all reports, presentations, and policy documents." *Id.*

FDA must take steps to ensure that its current study does not suffer from these same problems. If neither study shows an effect on "the broader U.S. population," then FDA could not possibly come up with *substantial* evidence that the graphic warnings directly advance FDA's interests. And if FDA issues the graphic warnings anyway, those warnings would be inherently arbitrary under the Administrative Procedure Act, 5 U.S.C. § 706(2)(A), and incapable of satisfying the government's burden for restricting speech under the First Amendment, *see R.J. Reynolds Tobacco Co.*, 696 F.3d at 1220.

Third, while the Agency has previously stated that it would take *at least* until November 2021 to issue a revised final rule that would pass muster under the First Amendment, FDA has now committed itself to submitting that same rule by May 2021—six months earlier than it had previously stated—as a result of ongoing litigation in the U.S. District Court for the District of Massachusetts. *See* Def.'s Statement Regarding Proposed Expedited Rulemaking Schedule at 2, *Am. Academy of Pediatrics v. FDA*, 1:16-cv-11985 (D. Mass. Oct. 5, 2018). In light of this expedited schedule, it is even more critical that the Agency provide impacted parties with the opportunity to meaningfully review and provide feedback on the proposed study. The expedited schedule leaves no room for error, and without satisfactory results from this study, FDA simply will not be able to satisfy its burden of providing *substantial* evidence that the proposed warnings directly advance a substantial interest under the First Amendment.

3. Given the Paperwork Reduction Act's clear purpose of facilitating transparency in the Agency's scientific endeavors, FDA must release, and solicit comments on, additional information about this proposed study. That information is critical to ensuring that the public and interested parties are capable of adequately reviewing and analyzing the study for the purpose of commenting on its quality and practical utility. For these same reasons, once the study is completed, FDA must promptly release the data that is generated by the study, so that the public and interested parties have sufficient time to review, analyze, and potentially attempt to replicate the results *before* FDA issues a proposed rule. Failing to take these steps would likely lead not only to another failed attempt to develop graphic warnings that can survive constitutional scrutiny, but also to a significant and unjustified expenditure of the Agency's personnel and monetary resources.

III. FDA's STUDY APPEARS TO CONTAIN SERIOUS METHODOLOGICAL FLAWS THAT WILL OVERSTATE THE EFFECTIVENESS OF THE GRAPHIC WARNINGS.

A. FDA has not shown that the study has an adequate sample size for each condition.

FDA's study also appears to have a relatively small sample size given the number of proposed conditions and related details regarding the study methodology. "Regardless of the motivation for [a] study, it is *essential* that it be of an appropriate size to achieve its aims." Elise Whitley & Jonathan Ball, *Statistics Review 4: Sample Size Calculations, Critical Care* at 1 (May 2002), https://tinyurl.com/y8rzdbmo (emphasis added). Indeed, in other contexts, FDA has recognized how important the concept of sample size is to a study. *See* FDA, *Draft Guidance: Applications for Premarket Review of New Tobacco Products* at 10 (Sept. 2011), https://tinyurl.com/yc5z42hy (explaining that, "for each study showing the health risks of [a] product, [the applicant] should include … [t]he statistical analysis plan including a detailed description of the statistical analyses used, including … the reason for [the] choice of sample size").

Here, FDA estimates that 7,460 adults and 2,300 adolescents will participate in the study. 83 Fed. Reg. at 48,627. But FDA plans to divide these individuals among 17 different conditions. *Id.* That means that approximately 439 adults and 135 adolescents will view each graphic warning. Such a small number will not support robust examination of the data by most demographic characteristics, and likely across other conditions being tested. This is readily demonstrated by FDA's announced intent to gather data from six different demographic groups, including

"[1] adolescent current cigarette smokers aged 13 to 17 years, [2] adolescent non-smokers who are susceptible to initiation of cigarette smoking aged 13 to 17 years, [3] young adult current cigarette smokers and [4] non-smokers aged 18 to 24 years, and [5] older adult current cigarette smokers and [6] non-smokers aged 25 years and older." *Id.* Once FDA breaks down the 17 conditions by six different demographic groups, the sample size is especially small—particularly for adolescents.

B. The study suffers from selection bias.

Although FDA has provided a dearth of information on how it plans to conduct the proposed graphic-warnings study, the limited information disclosed shows that the Agency's methodology suffers from selection bias. That bias is likely to have a significant impact on the reliability of the data and, in turn, the practical utility of the study. Moreover, commentators have pointed out this problem to the Agency numerous times in past graphic-warning studies, as described below. The Agency must correct this methodological flaw to ensure that the study actually produces valid and reliable data.

The selection-bias problem previously arose in 2010 when FDA issued a proposed graphic-warnings rule. In response to that proposed rule, RAIS submitted comments that described how the study underlying the rule suffered from selection bias. *See R.J. Reynolds Tobacco Co.*, 696 F.3d at 1210. Specifically, RAIS pointed out that the invitation to participate in the study identified its substantive focus and made clear that it was funded by FDA. *See* R.J. Reynolds Tobacco Company, *Comment on FDA's Proposed Rule for "Required Warnings for Cigarette Packages and Advertisements,"* Docket No. FDA-2010-N-0568, at 7 (Jan. 11, 2010). Under these circumstances, "one would not expect the sample selection effects to be neutral." *Id.* (quotation marks omitted).

This methodological flaw was compounded by FDA's failure to address the significant 32% dropout rate of study participants. *Id.* This failure was particularly problematic because it was unlikely that quitting the survey prior to completion was a random event; rather, such a significant dropout rate was more likely the result of smokers not being receptive to the graphic-warning messages. *Id.* Absent a correction for this methodological flaw, the results of that survey almost certainly overstated the likely effect of the warnings. *Id.* Rather than addressing this potential issue, however, "FDA avoided the substance of the argument by conceding that its study provides insight on the relative effectiveness of the various warnings under consideration, not on the absolute effects of the warnings in general." *R.J. Reynolds Tobacco Co.*, 696 F.3d at 1210 (quotation marks omitted).

The selection-bias problem arose again in FDA's more recent study of the textual warnings that might accompany the graphic images. As noted above, OMB determined that "significant limitations exist with regard to the generalizability of results from this study." *See* OMB Terms of Clearance. Specifically, OMB determined that "[r]ecruitment of the study sample from the online panel is also subject to bias resulting from potential differences between survey responders (i.e., panelists who received the invitation and opted to participate in [the] study) and non-responders (i.e., panelists who were invited but chose not to participate) in characteristics that may be associated with key study outcomes." *Id.* Because of this limitation (among others), OMB concluded that "the relationship between treatment and outcomes [that FDA] find[s] in [its] study *may not generalize to the broader U.S. population*." *Id.* (emphasis added).

FDA's proposed study suffers from the same problems. According to the September 26 notice, the proposed graphic-warnings study is a "voluntary online experiment" that appears to use convenience sampling from a population of more than 1.2 million people that are already enrolled in a pre-existing internet panel. 83 Fed. Reg. at 48,626–27. In other words, this study relies on the same sampling methodology that OMB has already said is subject to material selection bias and issues regarding whether the results of the study would even be generalizable to the broader U.S. population. *See* OMB Terms of Clearance.

Moreover, the social-desirability bias associated with smoking, as further described below in Section III.F, means that many potential participants may choose not to participate, thereby creating additional selection bias in the study. Indeed, 32% of survey participants did not complete FDA's 2010 graphic-warnings study, which suggests that these biases may have had a significant impact on FDA's previous study. A similar dropout rate here would present significant concerns because the investigator conducting a voluntary online study lacks the corrective measures available with a more adequately controlled study, such as the ability to identify factors that contributed to a participant dropping out and the ability to make adjustments to the study population to account for selection bias.

Finally, the selection-bias problem could be even worse than it currently appears. The information provided in the September 26 notice strongly suggests that the proposed study will suffer from selection bias. But FDA has not disclosed other important details about the study—such as the inclusion criteria that the Agency will rely on when screening potential survey participants. For example, it is not clear whether the Agency's only inclusion criteria are those related to the age of the population and their current use of cigarettes or whether potential participants will be screened based on additional criteria. Even if those are the only inclusion criteria for the study, FDA has not disclosed the criteria that it will use to determine that certain participants in the adolescent population are "susceptible to initiation of cigarette smoking," or if the Agency will simply conclude that all adolescent participants that are not current cigarette users are susceptible to initiation. These and similar criteria go directly to the question of selection bias, and without knowing the parameters that FDA intends to use, it is impossible for the public and interested parties to evaluate and provide feedback on potential flaws in the study methodology relating to the selection of study participants. Accordingly, in addition to addressing the existing issues of selection bias discussed above, RAIS requests that FDA disclose the inclusion criteria that the Agency plans to utilize in screening participants for the study.

C. The questions that FDA plans to ask create a serious risk of bias.

After showing the participants the graphic warnings, FDA plans to ask them a series of questions. 83 Fed. Reg. at 48,627. Once again, it is difficult to assess the questions that FDA plans to ask, given that FDA has not published them. (In particular, FDA does not say whether it will ask these questions separately about the textual warnings and the graphic images.) Nevertheless, FDA's broad description of those questions suggests that they are deliberately crafted to support a pre-ordained result: namely, that the warnings would "increase public understanding of the negative health consequences of cigarette smoking." *Id.* at 48,626. Each of the question topics suffers from this problem:

- ***"(a) if the information presented in the warning was new"***: Given that the text and graphic images will be different from the existing warnings, participants will know that the correct response is "yes."

- ***"(b) self-reported learning from the warning"***: This topic is even less of a test, as it simply asks the participants to repeat back the message that is in front of them.

- ***"(c) if the warning was easy to understand"***: The answer to this question will be the same as the previous answer—indeed, if the warning is hard to understand, there would not be any "self-reported learning."

- ***"(d) if the warning was perceived to be a fact or an opinion"***: The participants will know that the warning comes from FDA, which will lead them to say that the warning is perceived to be a "fact."

- ***"(e) if the warning was informative"***: The previous questions will bias the answer to this question: because FDA has already asked whether the warning was "new" and asked about "self-reported learning," participants will know that they are supposed to say that the warning was "informative." Moreover, the word "informative" is ambiguous; if it means "new," then this topic is wholly redundant of the first topic.

- ***"(f) if the warning grabbed their attention"***: This topic is yet another replay of whether the warning is "new." If participants see the warning as "new," then it will also "grab[] their attention"—particularly when the study directs participants to focus on that warning.

- ***"(g) if the warning made them think about the health risks of cigarette smoking"***: Given that the warning discusses the health risks of smoking, it will undoubtedly make the participants "think about the health risks of smoking."

As noted above, it is extremely difficult—if not impossible—to meaningfully critique these question topics, given that FDA has not published the actual questions that participants will answer before and after viewing the graphic warnings. Nevertheless, if FDA wants the study to provide a fair assessment of the warnings' effectiveness, then the Agency must take care to avoid biased questions such as these.

In addition, FDA will need to avoid question-order bias. Once a participant has been given information in a prior survey or interview question, the participant cannot take herself back to her pre-survey state of knowledge. *See* Statement of W. Kip Viscusi, Docket No. FDA-2010-N-0079, at 15 (Apr. 22, 2010), https://tinyurl.com/ycah2qh7 ("Viscusi Statement"). And that can influence the results. For example, if FDA asks about "self-reported learning" and *then* asks whether the warnings were "informative," the first question will likely bias the answer to the second question.

Finally, FDA should expand the questions that it plans to ask. In *R.J. Reynolds Tobacco Co.*, the D.C. Circuit found it relevant that the previous graphic images "could be misinterpreted by consumers." 696 F.3d at 1216. FDA should therefore ask participants whether the images

convey a different message than the textual warnings. The D.C. Circuit also found that the previous images were not "purely factual" because they "evoke[d] an emotional response." *Id.* FDA is on notice that it must ask the participants whether the new images evoke such a response.

D. The study protocols do not appear to adequately mimic real-world conditions.

In order to determine what effects (if any) the graphic warnings would have on the public, FDA should design its study to mimic real-world conditions to the greatest extent possible. Although FDA's failure to publish the study's protocols makes it difficult to assess them, FDA's brief overview of the study suggests that it will not adequately mimic real-world conditions.

First, the study overview says that, "[i]n the 16 treatment conditions, participants will view 1 graphic health warning." 83 Fed. Reg. at 48,627. In the real world, however, cigarette smokers would not be exposed to only a single warning; instead, they would be exposed to all of them over time. *See* 15 U.S.C. § 1333(c).

Second, by asking participants to specifically focus on the warnings, the study will likely overestimate their effects. That is particularly true given that the warnings are novel.

Third, the study overview says that "participants will view their assigned warnings both on a mock cigarette package and a mock cigarette advertisement." 83 Fed. Reg. at 48,627. In the real world, however, consumers would rarely view both the packaging and advertisements at the same time. By having the participants view two separate warnings simultaneously, the study may again overestimate the effects of the new warnings.

Fourth, the study overview says that the participants will view the graphic warnings once during Session 1 and once during Session 2, a day or two later. *Id.* Thus, the study does not measure whether consumers would get used to the warnings after viewing them repeatedly over a long period of time.

Finally, the study's 14-day gap in between Session 2 and Session 3 is problematic. That gap gives the participants time to do their own research about the risks of cigarettes, which could likewise overstate any effects a graphic-warnings rule might have. To avoid that possibility, FDA should instruct participants not to do any independent research during the study.

E. The study does not appear to include meaningful pretesting.

In addition, FDA's study appears to lack meaningful pretesting. "The importance of this critical step cannot be underestimated." *See* Theresa J. DeMaio et al., U.S. Bureau of the Census, *Improving Survey Quality Through Pretesting* at 1 (1998), https://tinyurl.com/ycndsu98. Indeed, "pretesting the instrument before it is actually administered may be the deciding factor in whether the survey is successful in meeting its objectives." *Id.*

FDA says that, "[p]rior to the main data collection, 2 sequential pretests, each with 50 participants, will take place to ensure correct programing of Session 1 and to identify any issues with the study design and implementation." 83 Fed. Reg. at 48,627. FDA estimates that this pretesting will take an average of 12 minutes per respondent, which is much less than the 25-minute reporting burden for the main data collection. *Id.* That suggests that the pretests will

simply be a check on whether the computerized survey runs correctly, and whether any serious implementation problems are encountered. *See* Viscusi Statement at 13. But that is not a meaningful pretest.

Instead, FDA should ask the participants to explain what the wording of the study's questions means to them and whether there are any ambiguities in that wording. *See* DeMaio et al. at 1–2 (explaining that one form of pretesting is "cognitive interviews," which "are a combination of having the respondent think aloud and having the interviewer probe for the respondent's definition of terms or concepts (e.g., 'what does the term quit smoking mean to you?') or interpretation of the question (e.g., 'can you tell me in your own words what this question means to you?')"). Such testing can help identify initial areas of confusion that require changes to the questions that FDA plans to ask. If pretesting reveals that confusion exists, then FDA should revise the questions and perform additional pretesting. *See* DeMaio et al. at 6 (noting that when "question revisions resulting from question pretesting do not get retested prior to inclusion in the production survey," it "is rarely known whether the expected benefit from the revision is realized").

FDA should also conduct pretesting to determine whether an Internet panel is the most appropriate method for this study. Although Internet surveys are useful for many issues, such surveys are not always well-suited to analyzing warnings that appear on a product. *See* Viscusi Statement at 12. Instead, examining the actual packaging is often a much more meaningful approach to assessing warnings than looking at warnings that are highlighted on a computer screen. *Id.* As a result, FDA should explore whether a different method—such as in-person interviews where the participants would be able to see and manipulate package mock-ups—would be more appropriate. *Id.* at 13. FDA could also consider combining the Internet aspect of the survey with a prior mailing of mock-ups of the test-product packaging, which the respondents could examine while taking the Internet survey. *Id.* at 12.

F. FDA must minimize the possibility of social-desirability bias.

When researchers ask about activities that are illegal or socially undesirable, participants have a tendency to offer the legal or socially desirable response. This effect, which is referred to as social-desirability bias, is a particular problem in the field of tobacco research. As one respected researcher explained decades ago:

> Given the widespread harassment of cigarette smokers and the evidence that smoking is actually dangerous to health, it is not surprising that smokers sometimes lie about their smoking. How better for a smoker to avoid the pestering of a physician or other interviewer than to say (whether believing it or not) that he wants to and has even tried to give up cigarettes? And, if the questioner asks if the attempts to stop have been serious, who would want to confess a half-hearted effort? Yet, answers to questions of 'wanting to stop' and 'trying to stop' have regularly been used uncritically—as if smokers now must be telling the truth.

Lynn Kozlowski et al., *What Researchers Make of What Cigarette Smokers Say: Filtering Smokers' Hot Air*, Lancet at 699 (Mar. 1980); *see also* Simon Chapman, *Smokers: Why Do They Start—And*

Continue?, 16 World H. Forum 1, 7 (1995) ("Plainly, social contexts in which smoking is increasingly vilified can produce a gap between what people feel obliged to say to researchers and what they genuinely feel."); Gary Giovino et al., *Trends in Cigarette Smoking Cessation in the United States*, 2 Tobacco Control S3, S9 (Supp. 1993) ("In 1991, 76% of current smokers stated that they wanted to quit, and the number hasn't changed much over time. Answering 'no' to this question is probably a socially unacceptable answer. We will need to consider that in our deliberations.").

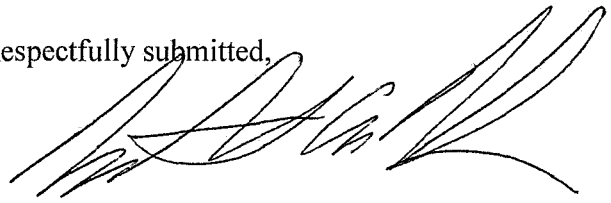
This type of bias could easily lead participants in FDA's study to give the "socially desirable" answers—that the graphic warnings present information that is "new," "informative," "grabbed their attention," or "made them think about the health risks of cigarette smoking." Once again, FDA must carefully design its study to minimize this form of bias.

* * *

As currently designed, FDA's study suffers from serious First Amendment problems and pervasive methodological flaws. Unless FDA makes the modifications set forth above, the study will have no chance of providing support for a graphic-warnings rule.

Thank you for your consideration of these important concerns.

Respectfully submitted,



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